

**Amendments to the Claims:**

**Listing of the Claims:**

The following claims replace all prior claim sets of the subject application.

Please cancel claims 2-5, 9-20, 31-32, 37, 43 and 45 without prejudice as to the subject matter contained therein.

1. (Currently amended) A method for growing islet producing stem cells (IPSCs), islet progenitor cells (IPCs) and IPC-derived islets (IdIs) comprising the steps of
  - a) culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of IPSCs and ductal epithelial cells and substantially lethal to differentiated cells in a basal medium comprising serum less than about 0.5%, and glucose less than about 1 mM, undisturbed for at least 3 weeks, whereby an epithelial monolayer containing IPSCs is produced, and
  - b) initiating cellular differentiation, whereby IPCs and IdIs are produced.

2-5. (Cancel)

6. (Original) An *in vitro* produced IPC-derived islet (IdI) comprising  $\beta$  cells and either  $\alpha$  or PP cells, wherein said  $\beta$  cells are located in the center of the IdI, said  $\alpha$  or PP cells are located in an outer cortex of the IdI, and proliferating and undifferentiated cells are located in an inner cortex of the IdI, wherein about 20 to 25% of the total cells of said IdI are  $\beta$  cells.

7. (Currently amended) An IdI comprising  $\beta$  cells located in the center of the IdI,  $\alpha$  or PP cells located in an outer cortex of the IdI, and proliferating and undifferentiated cells located in an inner cortex of the IdI, wherein about 20 to 25% of the total cells of said IdI are  $\beta$  cells, produced according to a method comprising the steps of:

- a) culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of IPSCs and ductal epithelial cells, and

substantially lethal to differentiated cells in a basal medium comprising serum less than about 0.5%, and glucose less than about 1 mM, undisturbed for at least 3 weeks, whereby an epithelial monolayer containing IPSCs is produced, and

- b) initiating cellular differentiation, whereby IPCs and IdIs are produced.

8. (Original) The IdI of claim 7 wherein said IdI is human.

9-20. (Cancel)

21. (Original) A method of treating pancreatic disease or producing a pancreas-like structure in a mammal which comprises implanting the IdI of claims 6 or 7 into a tissue of the mammal.

22. (Original) The method of claim 21 wherein the IdI is encapsulated in an insulin, glucagon and somatostatin permeable capsule.

23. (Original) The method of claim 22 wherein the capsule is hyaluronic acid.

24. (Original) The method of claim 21 wherein the IPSCs from which the IdIs arise, originate from an individual into whom the IdI is implanted.

25. (Original) The method of claim 21 wherein the pancreatic disease is insulin-dependent diabetes.

26. (Currently amended) A method of treating pancreatic disease or producing a pancreas-like structure in a mammal which comprises the steps of

- a) culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of IPSCs and ductal epithelial cells, and substantially lethal to differentiated cells, whereby a ductal epithelial monolayer containing IPSCs is produced,

b) initiating cellular differentiation, whereby IPCs and IdIs are produced,  
c) implanting in a mammal a composition comprising said IdIs and  
optionally cells or tissue selected from the group consisting of said ductal epithelium,  
IPSCs, and IPCs, IdIs and any combination thereof, whereby a pancreas-like structure and  
islet hormones are produced, providing for the treatment of the pancreatic disease.

27. (Original) The method of claim 26 wherein said composition is encapsulated  
before said implantation step.

28. (Original) The method of claim 26 wherein said implantation step comprises  
implanting into the mammal's pancreatic tissue.

29. (Original) The method of claim 26 wherein said implantation step comprises  
implanting into a subcutaneous pocket of the mammal.

30. (Original) The method of claim 26 wherein said implantation step comprises  
implanting beneath a kidney capsule in the mammal.

31-32. (Cancel)

33. (Currently amended) A method for analyzing the differentiation of pancreatic  
stem cells which comprises culturing *in vitro* the IPSC and ductal epithelium composition  
of claim 2 1(a).

34. (Original) The method of claim 33 further comprising the step of inducing said  
IPSCs to initiate differentiation into IPCs and IdIs, whereby stages of differentiation are  
identified.

35. (Original) The method of claim 34 further comprising the step of identifying  
mRNA or protein markers specific to a stage of differentiation.

36. (Original) The method of claim 35 wherein the markers are expressed on the cell surface, are secreted or are intracellular.

37. (Cancel)

38. (Currently amended) A method for long-term propagation of IPSCs which comprises serially transferring a cellular composition comprising IdIs and optionally material selected from the group consisting of ductal epithelium, ~~IdIs~~, IPSCs, IPCs and any combination thereof.

39. (Original) The method of claim 38 wherein said serial transfer involves the transfer of IdIs and IPSCs.

40. (Currently amended) A method for inducing neovascularization in a pancreatic implant in a mammal comprising transplanting into said mammal the pancreatic implant comprising IdIs and optionally cells or tissue selected from the group consisting of IPSCs, and IPCs and ~~IdIs~~, whereby vascularization is induced or enhanced.

41. (Currently amended) The method of claim 40 wherein the implanted tissue is only IdIs.

42. (Currently amended) A structure consisting essentially of a pancreas-like structure produced by implantation of IdIs and optionally cells or tissues selected from the group consisting of IPSCs; and IPCs and ~~IdIs~~, and comprising at least 50% by weight of endocrine tissue.

43. (Cancel)

44. (Original) The pancreas-like structure of claim 42 wherein said structure comprises endocrine cells arranged in IdIs or anatomically similar structures.

45. (Cancel)